LEFT VENTRICULAR DUAL-ENERGY SUBTRACTION ANGIOGRAPHY IN PATIENTS: A MOTION IMMUNE DIGITAL SUBTRACTION TECHNIQUE

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Left ventricular (LV) digital subtraction angiography (DSA) using the standard temporal subtraction technique is limited by misregistration artifacts caused by cardiac, respiratory and gross patient motion. Motion artifacts are particularly severe during temporal subtraction DSA exercise stress studies. Dual-energy DSA imaging, in which 30 Hz x-ray pulses alternate between 70 and 120 kVp, is insensitive to patient motion. In this initial patient study, the image quality of dual-energy DSA was assessed and compared with standard cine ventriculography. Eight patients, ranging in weight from 54-100 kg and in cardiac index from 2.4-4.3 L/min/m^2 (mean 3.5±0.7), underwent 30° RAO direct LV injection cine ventriculography. Fifteen minutes later 40 ml of Hypaque-76 was injected into the main pulmonary artery and 30° RAO dual-energy DSA images of the left ventricle were obtained. Subjective visualization of the left ventricular contour by dual-energy DSA was good in all cases, and image quality did not deteriorate with patient motion. To assess the ability to visually detect left ventricular endocardial borders by dual-energy DSA, LV end-systolic and end-diastolic volumes as determined by the area-length method using direct LV injection cine (C) and dual-energy DSA (DE) were compared. The regression line was DE=0.93 C + 4.6 ml. The r value was 0.96. The range of volumes was 15-216 ml. We conclude that dual-energy DSA from a pulmonary artery injection of contrast produces high spatial resolution images of the left ventricle, even in the presence of patient motion. The motion immunity of dual-energy DSA may allow for the assessment of left ventricular function during exercise in patients using a venous injection of contrast.

CARDIAC DONOR HEART DYSFUNCTION: EVIDENCE FOR CATECHOLAMINE-MEDIATED MYOCARDIAL INJURY

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Brain dead organ donors are occasionally eliminated from cardiac organ donation because of unexplained myocardial dysfunction. To test the hypothesis that massive sympathetic discharge may contribute to cardiac donor heart dysfunction (DHD), we examined the ß-adrenergic pathways of DHD hearts (age 17±2) identified by an abnormal echocardiogram (shortening fraction .18±.03). The contractile response (CR) to isoproterenol (ISO) and calcium (Ca^{2+}) were measured in isolated RV trabeculae. $ß_1$ and $ß_2$ receptor (R) subtypes were measured by radioligand binding and tissue catecholamines (CAT) were measured radioenzymatically. Results were compared to on-site donors not transplanted for reasons unrelated to donor organ function (age 37±3, p<.05 vs DHD): *p<.05

	CR, mg		ß R fmol/mg		Tissue Cat (ng/g)		
	ISO	Ca^{2+}	$ß_1$	$ß_2$	NE	EPI	DA
DHD	*880	862	*92.2	18.6	*1230	64	540
(n=7)	±134	±265	±6.6	±3.9	±249	±16	±132
Normals	1848	1218	71.2	18.6	658	48	457
(n=14)	±238	±200	±5.0	±1.8	±95	±7.0	±79

CONCLUSIONS: 1) Organ donors with unexplained DHD have a marked decrease in isoproterenol stimulated muscle contraction despite normal-increased $ß_1$ R levels. 2) This uncoupling of DHD ß-adrenergic R is consistent with exposure to high levels of adrenergic neurotransmitter, which may be the cause of DHD.

Tuesday, March 20, 1990
10:30AM–12:00NOON, Room 23
Cardiac Transplantation: Donor Allograft Physiology and Adaptive Responses

EVIDENCE FOR SYMPATHETIC REINNERVATION AFTER CARDIAC TRANSPLANTATION IN HUMANS

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Cardiac reinnervation after orthotopic transplantation (CT) occurs in animal models but human studies suggest that reinnervation does not take place.To more specifically determine if sympathetic reinnervation occurs in transplanted human hearts, we measured myocardial norepinephrine (NE) release [Δ[NE] in blood simultaneously obtained from the ascending aorta (Ao) and coronary sinus(CS)] at rest, after tyramine (an agent that causes degranulation of intact sympathetic nerve terminals, 0.55µg/kg, IV), and after sustained isometric handgrip.(a physiologic stimulus) in 3 patients <2 months after CT, 17 patients ≥1 year after CT, and 4 normal patients. The reproducibility of $Δ[NE]_{CS-Ao}$ measurements (radioenzymatic method) was assessed by comparing repeat measurements (n=12, mean absolute difference ±SD=39±41pg/ml), Evidence of reinnervation was defined as an intervention-induced increase in $Δ[NE]_{CS-Ao}$ by >3SD control (*i.e.*> 123pg/ml).

Results^: intervention	time after CT	basal $Δ[NE]_{CS-Ao}$	peak^ $Δ[NE]_{CS-Ao}$	ΔAP (mmHg) sys	dia	Δheart rate(bpm)
tyramine	<2mo	27±21	12±22	27±6	16±4	1±2
	≥1yr	48±15	439±78*†	19±3	9±2	4±1
	normal	42±41	1477±147*	31±9	9±7	9±7
hangrip	<2mo (n=2)		29±20	24±4	13±4	4±3
	≥1yr (n=6)		263±97*	18±4	22±3	2±3
	normal (n=3)		217±130*	22±5	10±7	9±7

^mean±SEM, + after intervention, *p<.05 vs. ≤2mo after CT, †p<.05 vs.normal

13 of 17 patients studied ≥1yr after CT had a significant transmyocardial release of NE after tyramine and all of those patients had a significant NE release during isometric hangrip ($Δ[NE]_{CS-Ao}$=340±113pg/ml). Conclusion: Early after CT the myocardium does not release NE, suggesting denervation. Late after CT, the majority of patients can release substantial, but subnormal, quantities of NE in response to tyramine and physiologic stimuli, suggesting that limited sympathetic reinnervation occurs in the majority of transplanted human hearts.

INCREASED EXPRESSION OF $ß_2$-ADRENERGIC RECEPTORS IN SURGICALLY DENERVATED, PREVIOUSLY TRANSPLANTED HUMAN VENTRICULAR MYOCARDIUM

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We have previously reported that the surgically denervated, transplanted human heart (TX) exhibits presynaptic supersensitivity to catecholamines but normal total ß receptor density. We now report measurement of ß receptor subtypes, tissue norepinephrine (NE) and adenylate cyclase (AC) in material prepared from right and left ventricular myocardium (VM) removed from transplant recipients with normal global LV function who were retransplanted for graft atherosclerosis (±SEM): *p<0.05

Group (n)	Receptor Density, fmol/mg			AC, pmol cAMP/min/mg			NE ng/g
	Total ß	$ß_1$	$ß_2$	ISO	NaF	Forsk	
TX	93.6	62.2	31.0*	40.4*	38.7	219	47*
(10)	±12.4	±9.0	±5.1	±3.1	±4.6	±22	±19
NL†	94.7	75.2	18.6	30.5	35.6	238	817
(68)	±3.6	±3.3	±1.4	±1.6	±2.0	±12	±92

†normal innervated VM from organ donor controls; ISO=isoproterenol; Forsk=forskolin; NE=norepinephrine

CONCLUSION: TX contains an increased density of $ß_2$ adrenergic receptors. Since the AC response to ISO is mediated predominantly by $ß_2$ receptors in human VM, the increased $ß_2$ population appears to be coupled to a functional response. Thus TX is not only supersensitive to circulating epinephrine by virtue of denervation and loss of $uptake_1$, but the $ß_2$ "epinephrine receptor" is also increased in density in TX VM.